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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,323	01/25/2002	Harry R. Davis	CV01489K	1525

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PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 05/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,323	DAVIS ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-101* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,11-13,21,28,32,34,37-40,42,43,47,48,83,84,86,100 and 101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

PD

DETAILED ACTION

In view of the appeal brief filed on January 12, 2005, PROSECUTION IS HEREBY REOPENED. New ground of rejections are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claims 35-36, 41, 49-52, 55, 57, 60, 62, 65, 67, 70, 72, 75, 77, 80, 82, 85, 87, and 92 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in response filed November 21, 2003.

Claims 5-10, 14-20, 22-27, 28-31, 33, 44-46, 53-54, 56, 58-59, 61, 63-64, 66, 68-69, 71, 73-74, 76, 78-79, 81, 88-91, and 93-99 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in response filed November 21, 2003.

Claims 1-4, 11-13, 21, 28, 32, 34, 37-40, 42, 43, 47-48, 83-84, 86, and 100-101 have been examined herein to the extent they read on the elected invention and species.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 100-101 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 10/057,646 ('646). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-4 of '646 teaches a pharmaceutical combination comprising ezetimibe (azetidinone compound) and niacin (a vitamin).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37, 48, and 86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the instant case, the claims herein are not enabled for the prevention of vascular diseases, obesity, diabetes, and other diseases recited herein.

The claims are directed to a composition of preventing the vascular conditions comprising sterol absorption inhibitor, PPAR activator, and nicotinic acid derivatices. The specification fails to adequately teach how to use the herein claimed composition to prevent the any vascular event. It is well-known in the state of the art that vascular conditions encompass various cardiovascular disorders such as hypertension, acute myocardial infarction, unstable angina, endocarditis, and even arrhythmia, such as ventricular fibrillation. These conditions are caused by various etiologies. See, Merck Manual, 16th ed., 1992, page 365-367, table of content for cardiovascular disease. Please note that even a basic reference, such as Merck Manual, has over 200 pages of information with regard to cardiovascular disease. The instant claims are so broad that it encompasses the method of preventing **all** vascular disorders. The current known treatments of these disorders depends on the patient populations and the severity of the

disorders. Some of the disorders, such as primary hypertension, have no known etiology (See Merck manual, page 413). Thus, it is clear from the evidence of the Merck Manual that the ability to prevent vascular condition is highly unpredictable and has met with very little success. Applicants have not provided any convincing evidence such as working examples that their claimed invention is indeed useful as preventive for the first occurrence of vascular condition and have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 11-13, 37-40, 42, 43, 47-48, 83-84, and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US Patent 5,846,966) and Medical Letter (The Medical Letter on Drugs and Therapeutics, 1998, 40;1030:68-69), references of record.

Rosenblum et al. also teaches the elected compound herein, ezetimibe, useful for reducing cholesterol and the risk of artherosclerosis (See the abstract, also col. 32, Example 6, Compound 6A, and col. 40, line 52 particularly).

Medical Letter teaches fenofibrate as useful in reducing serum cholesterol level (See page 68 – 69).

The references do not expressly teach a composition containing fenofibrate and ezetimibe together.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate both ezetimibe and fenofibrate together in a single composition.

One of ordinary skill in the art would have been motivated to incorporate both ezetimibe and fenofibrate together in a single composition. The prior art teaches that both ezetimibe and fenofibrate as useful in reducing serum cholesterol individually. Therefore, combining two agents, which are known to be useful to reduce serum cholesterol individually, into a single composition useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

Claims 21, 28, 32, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. and Medical Letter as applied to claims 1-4, 11-13, 21, 28, 32, 34, 37-40, 42, 43, 47-48, 83, 86, and 100-101 above, and further in view of Katzung (Basic & Clinical Pharmacology, 6th ed., 1995, page 529), references of record.

Rosenblum et al. and Medical Letter suggest a composition containing fenofibrate and ezetimibe.

Rosenblum et al. and Medical Letter do not expressly teach the composition contains niacin.

Katzung teaches niacin as useful for lowering cholesterol (See page 529, col. 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate niacin into the fenofibrate – ezetimibe composition.

One of ordinary skill in the art would have been motivated to incorporate niacin into the fenofibrate – ezetimibe composition. All three ingredients, i.e., niacin, fenofibrate, and ezetimibe, are known as useful in reducing cholesterol. Therefore, combining two or more agents, which are known to be useful to reduce serum

cholesterol individually, into a single composition useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

Claims 100 and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US Patent 5,846,966) and Katzung, references of record.

Rosenblum et al. also teaches the elected compound herein, ezetimibe, useful for reducing cholesterol and the risk of artherosclerosis (See the abstract, also col. 32, Example 6, Compound 6A, and col. 40, line 52 particularly).

Katzung teaches niacin as useful for lowering cholesterol (See page 529, col. 1).

The references do not expressly teach a composition containing niacin and ezetimibe together.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate both ezetimibe and niacin together in a single composition.

One of ordinary skill in the art would have been motivated to incorporate both ezetimibe and niacin together in a single composition. The prior art teaches that both ezetimibe and niacin as useful in reducing serum cholesterol individually. Therefore, combining two agents, which are known to be useful to reduce serum cholesterol individually, into a single composition useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

Response to Arguments

Applicant's rebuttal arguments in page 8 to 10 in the Brief filed January 12, 2005 averring the cited prior arts' failure to provide suggestion or motivation to combine the herein claimed actives into a single combination or composition are not convincing. The motivation to combine is based on the fact that the herein claimed agents are useful to reduce serum cholesterol individually. It flows logically to combine two or more old and well-known agents, known to be useful as cholesterol-reducing agents, into a single composition useful for the very same purpose (See *In re Kerkhoven* 205 USPQ 1069).

Applicant's arguments in pages 10 and 14 of the Brief filed January 12, 2005 averring Medical letters teaches the LDL lowering activities of fenofibrate is not as effective as statins are not convincing. The fact is that fenofibrate can effectively reducing LDL cholesterol, in addition with its triglyceride lowering activities. Whether it is less effective in lowering cholesterol when comparing to the statins is irrelevant to the ground of rejections set forth in the previous office action mailed September 20, 2004. As discussed there and above, the motivation to combine is based on the fact that the herein claimed agents are useful to reduce serum cholesterol individually. It flows logically to combine two or more old and well-known agents, known to be useful as cholesterol-reducing agents, into a single composition useful for the very same purpose (See *In re Kerkhoven* 205 USPQ 1069).

Applicant's arguments in page 11 of the Brief filed January 12, 2005 averring the cited prior art's failure to teach a triple-combination composition since claim 32 would need an additional agent are not convincing. Niacin is a well-known vasodilator. It is evidenced in Katzung, a basic textbook, that niacin could cause vasodilatation in

cutaneous site and hypotension. Such vasodilatation effect of niacin is well-known in the art.

Applicant's rebuttal arguments in pages 11 and 14 in the Brief filed January 12, 2005 averring potential drug-drug interaction between fenofibrate and statins are not convincing. Drug-drug interactions exist between fenofibrate and statins or gemfibrozil and statins do not necessary mean that drug-drug interactions exist between fenofibrate and ezetimibe since ezetimibe is not a statin. Furthermore, such arguments are not directed to what is recited in the claims. Arguments directed to unclaimed limitations are considered moot.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5-10,14-20,22-31,33,35,36,41,44-46,49-82,85 and 87-99.